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Self-reported anxiety and sleep problems in people with epilepsy and their association with quality of life

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ABSTRACT

Comorbidities are common in epilepsy, and their role in quality of life (QOL) is receiving increasing scrutiny. Considerable attention has been focused on the role of depression, the most common comorbidity, with rather less attention paid to its frequent concomitant, anxiety, and other conditions known to be at increased prevalence among people with epilepsy (PWE) when compared to the general population. In this paper, we report findings from a UK-based survey in which we examined self-reporting of two common comorbidities, anxiety and sleep problems, factors associated with them, and their role in QOL in people with and without epilepsy.
Data were obtained via mailed questionnaires, supplemented by an internet survey, from PWE and age- and gender-matched controls. Based on self-reported symptoms, PWE were at higher risk of anxiety and sleep problems. Contributory factors for anxiety included poorer general health, worry about seizures, and self-reported antiepileptic drug (AED) side effects. Good social support emerged as protective for anxiety in PWE. Nighttime sleep problems were very common even in controls but were further elevated in PWE. Antiepileptic drug adverse events emerged as an important contributory factor for sleep problems. Trait anxiety emerged as significant for defining overall QOL, and its importance over state anxiety supports the notion of anxiety in PWE as a primarily premorbid condition. In contrast, sleep quality was not consistently predictive of QOL. Our study has important implications for clinical management, emphasizing the need for a holistic approach to address wider patient-reported problems as well as any epilepsy-specific ones.

1. Introduction

A diagnosis of epilepsy can have major negative implications for an individual's quality of life (QOL) and be associated with an increased risk of psychological problems [1,2]. To date, the most commonly explored factor implicated in reduced QOL of people with epilepsy has been seizure frequency: it has been reported that the vast majority of individuals who enjoy seizure freedom do not have lower QOL scores in comparison to the general population [3–5] while for those continuing to experience seizures, their QOL can be severely adversely affected [6]. Jacoby et al. [7] reported that in patients with new-onset seizures treated with antiepileptic medication, 2-year QOL profiles were enhanced compared to baseline for patients experiencing a single seizure only or entering an early remission and further impaired for patients experiencing late remission or a relapse to seizures. Spenser et al. [8] reported similar patterning of QOL among patients with epilepsy treated surgically, some of whom remained seizure-free subsequently while others experienced a recurrence of seizures. Seizure freedom, then, has been shown to reduce the 'intrusiveness' of epilepsy for QOL [9]; however, among potentially relevant clinical variables, seizure frequency alone has not been able to adequately account for observed impairments in QOL. Other potentially important predictors of QOL scores include seizure severity [10], seizure type [11], type of epilepsy [12], and treatment-related side effects [6,13].

While it is undeniable that its clinical features can have a major impact on QOL, a more recent alternative line of enquiry has aimed at examining the effects of the various comorbidities associated with having epilepsy. Strine et al. [14] reported on the prevalence of psychological and physical comorbidities in a large community sample in the US. Psychological distress including serious mental illness and major physical health problems were both more commonly reported by individuals identifying themselves as having a history of seizures than by nonaffected individuals as were other markers of impaired QOL such as not being in employment. Pulsipher et al. [15] reported a significant association between decreasing overall QOL and physical and psychological comorbidities, with these jointly accounting for around 14% of the variance in QOL scores. The differential effects of the different types of comorbidity were also highlighted by these authors — comorbid

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psychological conditions being more strongly predictive of scores for life satisfaction, epilepsy-related effects, and cognition and medical comorbidities being more strongly predictive of physical function and role limitations.

Anxiety and depression are the most commonly reported psychological problems among individuals with epilepsy [1,15–18]. For example, in the US 2004 HealthStyles Survey [18], those classifying themselves as having been affected by epilepsy were also twice as likely to report anxiety or depression as were other respondents and those classifying themselves as having active epilepsy were three times more likely to do so. Johnson et al. [19] set out to investigate the impact of anxiety and depression, as markers of psychological well-being, on health-related QOL and found that both exerted negative impacts. Furthermore, anxiety and depression emerged as more powerful predictors of QOL scores than did seizure frequency and severity. Similarly, Cramer et al. [20] found that both anxiety and depression significantly reduced QOL scores and the more severe they were, the more effects were noted on QOL measures.

However, it should be noted here that estimates of the incidence of both these psychological problems have varied widely [16,17,21,22]. Further, it is recognized that rates of psychological comorbidity are likely underestimated since an individual may be experiencing problems that are not made evident to the clinician. O'Donoghue and colleagues [23] found that only a third of those who could be classed as experiencing definite or borderline anxiety or depression based on their responses on a self-reported measure had psychological symptoms reported in their medical files.

Historically, much less attention has been given in the literature on epilepsy and QOL to prevalence and impact of anxiety problems than to depression [24]. For example, in a textbook published in 2000 on 'problem-solving in clinical practice', Schmitz [25] addresses the management of psychoses, depression, and suicidal behavior but not that of anxiety problems. In the context of epilepsy, anxiety may exist in its own right or be related to chronic features of epilepsy, be experienced only as part of a seizure, or be a more long-standing problem and patients can have symptoms which would fall under the category of generalized anxiety — persistent worrying about relatively minor matters [26].

Jacoby and colleagues [1,4] found that self-reported anxiety levels in a large community population of PWE differed markedly according to seizure frequency and correlated strongly with other QOL measures such as perceived impact of epilepsy and felt stigma. De Souza and Salgado [27] found levels of anxiety to be unrelated to either epilepsy or treatment variables or sociodemographic characteristics such as gender. It has been noted [28] that as in the general population, individuals with epilepsy may have varying susceptibility to developing psychological disorders such as anxiety. Johnson et al. [19] have cautioned that the emphasis that has been seen on depression in epilepsy should not eclipse the important role of anxiety for QOL of people with epilepsy since it exerts its own independent effects. In their own study, self-reported anxiety accounted for more than 30% of the variance in QOL scores (similar to the amount of the variance explained by self-reported depression) and independently predicted QOLIE-89 cognitive, physical health, and mental health subscale scores.

Sleep complaints are a frequent concomitant of anxiety disorder [29], and compromised sleep is known to be common among PWE [30,31]. Interactions between epilepsy and sleep have been found to take a number of different forms, including delay in sleep onset, difficulty staying asleep, or waking up too early [31], and have been associated with a number of potential causes, including insufficient sleep syndrome, poor sleep hygiene, coexisting sleep disorders, the effects of seizures themselves, and the effects of AEDs [32]. A large study by De Haas and colleagues [33] showed that over a 6-month period, PWE had twice the prevalence of subjective sleep disturbance as controls and that the presence of sleep disturbance was associated with a significant reduction in QOL beyond that attributable to just having epilepsy. In the general population, sleep disturbance creates huge demand for health-care services and huge use of over-the-counter medication [34]. Importantly, sleep disorders may also be indicators of major anxiety and depression [35].

Though Hermann [36] included sleep in his list of key domains of QOL for PWE, far less attention has been paid by researchers to this aspect of living with epilepsy than to anxiety or depression. As a result, the literature remains sparse and contradictory — despite that the role of sleep problems in impaired QOL is highlighted by patients with epilepsy themselves as are their concerns over the possibility that drug treatment may create or exacerbate problems with sleep [37]. Such concerns appear justified by a small but convincing literature identifying the quite differing effects that AEDs can have on sleep quality [31,32]. It has been argued that, like anxiety, sleep problems which are common in PWE are frequently missed by clinicians [32]. Sleep problems appear particularly common in patients experiencing partial seizures [33,38,39]. Both excessive daytime sleepiness [40,41] and obstructive sleep apnea [41] have been found to be more frequent in patients with epilepsy than in neurology patients without epilepsy and the general population.

That the complex relationship between epilepsy and anxiety and its frequent concomitant, sleep complaints, requires further investigation was the starting point for the work reported here. The overall aim of the study was two-fold: to examine rates of self-reported anxiety and sleep problems in people with epilepsy (PWE) and to explore contributory factors. Specifically, our objectives were as follows:

i. To compare levels of self-reported anxiety and sleep problems in PWE with those in controls to gain appreciation of the size of the problem in this patient group;
ii. To define the nature and extent of self-reported anxiety and sleep problems in two separate cohorts of PWE;
iii. To investigate the relationship of self-reported anxiety and sleep problems to a range of epilepsy-related and other factors;
iv. To identify from a broad range of possible predictors the most powerful predictors of anxiety and sleep problems reported by PWE;
v. To explore the relationship between anxiety and sleep problems and overall QOL in PWE.

2. Methods

2.1. Data collection strategies

A postal approach was used for data collection. The advantages of such an approach are well rehearsed in the literature [42], and we had successfully used it for collection of QOL information, including measures of psychological distress, previously [3,4,6,43–45]. People with epilepsy were recruited from two separate sources: the patient database of a large tertiary care center for epilepsy in North West England and the membership database of the UK national patient organization, Epilepsy Action (EA). To maximize recruitment from the EA sample (since previous work suggested that it might be less easy to recruit), the postal approach was supplemented by two other approaches described below.

2.2. Details of measurement instruments included in patient and control questionnaires

Two separate self-completion questionnaires were developed – one for people *with* and one for people *without* epilepsy – using previously validated scales, as detailed in Table 1, to ascertain for all respondents the presence/absence of anxiety disorder, daytime and nighttime sleep problems, degree of social support, overall health status and any (other) long-term health problems, and sociodemographic status (as described by age, gender, educational and occupational status). Additionally, the PWE questionnaire contained questions about possible medication side effects, worry about seizures, and perceived impact

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Table 1
Questionnaire content.[a]

Domain	Measure	Items and scoring	Evidence supporting use	Included in MC questionnaire
Anxiety	State–Trait Anxiety Inventory (STAI; Spielberger and Guillér-Riquelme and Buela-Casal [46–49])	40 items (20 'state' and 20 'trait'); 4-point scale to examine symptom intensity. Total score of 20–80 for both state anxiety and trait anxiety; higher score indicative of problem severity	Well validated and widely used in psychological and clinical research	Yes
Sleep	Pittsburgh Sleep Quality Index (PSQI, Buysse et al. [29])	19 items to assess nighttime sleep quality over a 1-month period; seven 'component' scores for sleep quality, latency, duration, efficiency, and disturbances, medication use, daytime dysfunction and a global score. Total score range of 0–21; higher score indicative of a problem	Validated for use in psychiatric and general medical settings and in clinical research and epidemiological studies	Yes
	Epworth Sleepiness Scale (ESS, Johns, MW [50,51])	8 items to measure excessive daytime sleepiness; 4-point scale to examine the sleepiness intensity in eight different situations. Total score range of 0–24; score of 10 or higher indicates that specialist help is required.	Shown to have high reliability (internal consistency, test–retest); factor analysis confirmed a single factor in both patients and controls	Yes
Medication effects	Liverpool Adverse Events Profile (Gilliam et al. [52])	19 items relating to side effects associated with AEDs. 4-point response ('never' to 'often/always' a problem in the last month). Total score range of 19–78; higher scores indicative of more severe SEs	Shown to detect significant differences in types of SEs reported, depending on the individual's drug therapy (Baker et al. [6])	Yes
Perceived impact of epilepsy	Impact of Epilepsy Scale (Jacoby et al. [43])	12 items covering relationships with spouse/partner, other close family members, and friends, social life/social activities, health, work/standard of living, feelings about self, plans/ambitions, driving, and independence. Total score range for this instrument of 12–60; higher scores indicating worsening effect of epilepsy	Original scale widely used; good evidence of validity/reliability of original version; recently revised and revalidated, revised version shown to have good psychometric properties	No
Perceived stigma	3-Item epilepsy-specific scale (Jacoby [53])	Dichotomous yes/no response; total score range of 0–3 (sum of positive responses); higher score indicating more severe stigma	Original scale widely used; recently revised version revalidated and shown to have good internal consistency, good concurrent validity, and reduced floor/ceiling effects	No
Social support	Social Support Scale (Sherbourne and Stewart [54])	19 items exploring perceptions of support across four domains: emotional/informational, tangible, affectionate, and positive social interaction and 5-point response from 'none of the time' to 'all of the time'. Data can be analyzed using domain scores or an overall social support index score.	Developed for use in US Medical Outcomes Study (MOS) of patients with chronic conditions; validation exercise in 2987 patients supported scale dimensionality, overall index score, reliability ($\alpha > 0.91$), stability over time, and construct validity	Yes
Seizure worry	Seizure worry scale (Abetz et al. [55])	2 items relating to past/possible future seizures; 4-point scale from 'not at all' to 'a lot'	Validation exercise reported by Abetz et al. [55]; scaling success high; negligible floor/ceiling effects; high reliability and validity	No

[a] Copies of the questionnaires are available, on request, from the authors.

and stigma of epilepsy (Table 1). The PWE questionnaire also included single items relating to the following: seizure classification (as only tonic–clonic, only other types, or both tonic–clonic and other types); estimated monthly seizure frequency; perceived level of seizure control; epilepsy duration; and drug type.

2.2.1. The State–Trait Anxiety Inventory (STAI [46])

The STAI is a self-administered 40-item measure (20 items relating to 'state' anxiety and 20 items relating to 'trait' anxiety; see E-Appendix 1). This measure has been shown to clearly differentiate between state anxiety, which its developers define as a temporary phenomenon, being a function of the stressors acting on an individual at a point in time, and trait anxiety, which they define as referring to 'relatively stable individual differences in anxiety proneness'. Levels of state anxiety are likely to be high in circumstances perceived by an individual to be threatening and irrespective of the objective danger (which may be the case for people experiencing seizures) and low in nonstressful or nonthreatening situations. In contrast, trait anxiety reflects a general and long-standing tendency to perceive situations as threatening or dangerous. Spielberger [47] notes that persons with higher trait anxiety scores also tend to have higher state anxiety scores.

The STAI uses a 4-point scale (not at all to very much so; almost never to almost always) to examine the intensity of anxiety symptoms. It has been well validated and widely used in psychological and clinical research. Total scores for both state anxiety and trait anxiety range from 20 to 80, with a higher score being more indicative of the severity of the problem. Internal consistency has been shown to be high for both domains (*alpha* coefficients of 0.90 and 0.93 for scores on the trait and state scales, respectively); test–retest coefficients have been shown to be higher for trait than state anxiety (0.73 to 0.86 and 0.16 to 0.62, respectively) [48], a finding which its author attributes to the transitory nature of state anxiety. In a recent meta-analysis involving over 150 studies, the authors concluded that the STAI clearly differentiates between people with anxiety and general populations and demonstrates high reliability (0.87–0.93) for patients across a range of anxiety disorders [49].

Sleep problems were assessed using two separate measures: one focusing on nighttime and the other on daytime sleep problems.

2.2.2. The Pittsburgh Sleep Quality Index (PSQI [29])

The PSQI is a 19-item self-rated questionnaire, assessing sleep quality and disturbances over a 1-month period (see E-Appendix 2). Patients' responses generate seven 'component' scores for subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of medication, and daytime dysfunction and a global score. It has been validated for use in psychiatric and general medical settings and in clinical research and epidemiological studies. The total score ranges from 0 to 21 with a higher score being more indicative of a problem. The PSQI has been shown to have acceptable levels of internal consistency (overall reliability coefficient of *alpha* = 0.83) and test–retest reliability, examined using paired *t*-tests and correlation coefficients, and of diagnostic sensitivity and specificity (kappa = 0.75, $p < 0.001$) in distinguishing between good and poor sleepers [29].

2.2.3. The Epworth Sleepiness Scale

The ESS is a self-rated questionnaire intended to measure excessive daytime sleepiness ([50]; see E-Appendix 3). The ESS uses a 4-point

scale (0 = no chance of dosing, 1 = slight chance of dosing, 2 = moderate chance of dosing, and 3 = high chance of dosing) to examine the intensity of dosing in eight situations. Subscores are added together to provide a total score. The total score for the ESS ranges from 0 to 24, with a score of 10 or over being an indication that specialist help is required. The scale has high internal consistency (Cronbach's *alpha* = 0.88) and high test–retest reliability ($p < 0.001$; [51]).

Other measures included in the PWE questionnaire were as follows: the Liverpool Adverse Events Profile [6,52], to examine reported medication-related side effects; the Impact of Epilepsy Scale [43], to assess perceived impacts on daily life; the Epilepsy Stigma Scale, to assess perceived stigma [53]; a measure of perceived social support [54]; and a measure of worry about past/possible future seizures [55]. Details of all these measures are provided in Table 1.

2.3. Target populations and recruitment process

Our target populations were PWE from the two sources outlined above and their age- and sex-matched controls (MCs).

2.3.1. The tertiary center sample

Five hundred and fifty (550) adults with active epilepsy (defined as at least one seizure of any type in the previous twelve months) and meeting prespecified inclusion criteria were identified from the tertiary center database, which contains clinical and demographic details of over 6000 patients. Each patient was mailed a study pack containing an introductory letter, a patient information sheet, a copy of the PWE questionnaire, and a prepaid return envelope. The study pack also included a separate envelope (an MC mail-out pack) containing a copy of the MC questionnaire and other parallel study documentations. In their introductory letter and information sheet, PWE were invited to identify an age- (within five years) and sex-matched control, who was not a cohabitee and who did not, to their knowledge, have epilepsy or take AED medication for any reason, and were asked to pass on to this person the MC mail-out pack.

Those approached were asked to return the questionnaire within 2 weeks even when no MC could be identified. Patients were sent a reminder if they did not return the questionnaire within 3 weeks; the method of approach adopted for controls precluded any reminders being sent out to them. All participants were asked to return completed questionnaires to the study office in the Division of Public Health at the University of Liverpool.

2.3.2. The Epilepsy Action sample

One thousand potential participants were identified via the Epilepsy Action (EA) Support Group membership database. Since the EA database does not distinguish between members with and without epilepsy, self-completion questionnaires (one for PWE and one for MCs) together with an explanatory letter and instructions on questionnaire completion were mailed to a sample of EA members. Reply-paid envelopes were enclosed for return of the questionnaires directly to the study office. Recipients who were themselves PWE were asked to identify an age- (within five years) and sex-matched control, who was not a cohabitee and did not, to their knowledge, have epilepsy or take AED medication for any reason. They were asked to pass on to this person a copy of the MC questionnaire. Recipients who did not themselves have epilepsy were asked to pass the complete questionnaire pack on to an adult (18 years and above) with epilepsy if they knew one. This sampling strategy made sending reminders to nonresponders not feasible.

The postal approach was supplemented by use of Internet approaches. Information about the purpose of the study, including the aims, objectives, and methods, was posted on EA's webpage. Users of the site with an interest in participating in the study were able to select a link to one of the two questionnaires, the PWE questionnaire or the MC questionnaire, which they were able to complete online and submit electronically to the study office. Additionally, information about the study was published in EA's June 2008 Newsletter. Those readers with an interest in participating in the study were asked to complete an 'expression of interest' slip enclosed in the newsletter and to return it to the study office in the prepaid envelope provided. The appropriate explanatory letter and questionnaire (PWE or MCs) were then forwarded to those registering their interest. No reminders were sent.

All returned questionnaires were reviewed to ensure that inclusion criteria were met and to check for completeness before being cleaned and coded prior to analysis.

2.4. Statistical analysis

Using the measures outlined above, we assessed the prevalence of anxiety and sleep disorders in both groups of respondents (PWE and MCs). In addition, we examined anxiety and sleep disorders in people with epilepsy in relation to variables cited as predictive factors in previous studies. Analyses were conducted using the statistical software package SPSS 17.0 and included the following:

i. Simple descriptive statistics
ii. Correlation analysis to explore relationships between variables
iii. Univariate and multivariate regression analyses to explore the predictive power of the independent variables for anxiety and sleep problems. Variables that were identified as being significant predictors of the outcome variable of interest in the univariate analysis were carried forward into a multivariate analysis to explore how these variables related to the outcome of interest when considered in combination. The multivariate regression analyses used the forward stepwise approach, with a significance value of $p < 0.05$ for inclusion in the models and a value of $p < 0.1$ for exclusion.

2.5. Ethical considerations

The study was externally reviewed and approved by the relevant UK committees (University of Liverpool Ethics Committee, Liverpool NHS Research Ethics Committee, and Hospital Trust Research & Development Committee).

3. Results

3.1. Response rates

Nine hundred and forty-seven PWE (196, hospital-based cohort; 751, EA cohort) and 297 matched controls returned completed questionnaires (Table 2), giving a response rate for the hospital patient sample of 35.6% and for the EA sample of 51.5%.

3.2. Characteristics of participants

People with epilepsy differed from controls across a range of sociodemographic characteristics (see Table 3). Both patient groups were younger than controls and more likely to be male, significantly less likely than controls to be married or cohabiting, and more likely to be single. Both patient groups were significantly less likely than controls to be in paid employment and significantly more likely to be unemployed. Controls were less likely than either of the groups with epilepsy to report other long-term health problems. There were also differences *between* the two patient groups for all sociodemographic characteristics other than the number of prescribed medications (see Table 3): fewer of the hospital sample were married or cohabiting and fewer were in paid work; conversely, a smaller percentage in the hospital sample than in the EA sample reported having other long-term health problems.

Comparing the two samples with epilepsy for clinical characteristics, the hospital-based sample had more severe epilepsy than the EA

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Table 2
Achieved participant sample size per cohort.

Cohort	Approached		Responded		Excluded[a]		Total achieved samples	
	PWE	Control	PWE	Control	PWE	Control	PWE	Control
Hospital-based	550	550	229	39	33	0	196	39
Epilepsy Action members*	1000		771	264	20	6	751	258
Combined sample totals							947	297

[a] 53 PWE and 6 controls were excluded from the analysis because of poor questionnaire completion (50% or more data missing).
* Controls identified by EA members - see methods section.

membership sample. In accordance with the inclusion criteria specified for the hospital sample (that they should have *active* epilepsy and be on AEDs currently), none of the hospital-based cohort had been seizure-free in the previous 12 months compared to more than a quarter of the EA sample and a significantly higher proportion of the hospital sample had experienced four or more seizures over that period (Table 3). Hospital-based patients also reported a higher average number of seizures per month than did EA members and were more likely to be taking AEDs currently and to be on polytherapy.

3.3. Reported anxiety and sleep problems in PWE and controls

Our first objective was to compare levels of self-reported anxiety and sleep problems in PWE with those in controls to gain appreciation of the size of the problem in this patient group. Controls had significantly lower median scores for both 'state' anxiety and 'trait' anxiety than did people with epilepsy (Table 4). Nighttime sleep problems were more commonly reported by people with epilepsy (by 79% of the EA patient sample and 67.1% of the hospital sample compared to 62.0% of controls). Patients with epilepsy were also significantly more likely than controls to report problems with daytime sleepiness ($p < 0.001$). Controls were significantly more likely than PWE to describe their health in general as 'excellent' or 'very good' and significantly less likely to consider their health now as worse than a year ago. Median AEP scores were lowest for controls. Overall QOL was rated higher by controls, with over three-quarters of the controls describing themselves as happy with their QOL compared to only around a half of people with epilepsy (Table 4).

Table 3
Sample sociodemographic and clinical characteristics.

	Epilepsy Action N = 751	Hospital-based n = 196	p-Value for differences between groups with epilepsy	Controls n = 297	p-Value for differences between groups with epilepsy and controls
Gender = male	283 (38.1%)	95 (49.5%)	0.004[a]	91 (31.1%)	<0.001[a]
Median age (IQR)	45 (21)	43 (19)	0.003[b]	51 (22)	<0.001[b]
Marital status					
Married/with partner	400 (53.6%)	85 (43.4%)	0.03[a]	207 (70.2%)	<0.001[a]
Divorced/separated	82 (11.0%)	21 (10.7%)		28 (9.5%)	
Widowed	29 (3.9%)	6 (3.1%)		12 (4.1%)	
Single	228 (30.6%)	79 (40.3%)		44 (14.9%)	
Employment status					
In paid work (FT/PT)	270 (36.9%)	42 (22.7%)	0.001[a]	185 (64.2%)	<0.001[a]
Unemployed	60 (8.2%)	17 (9.2%)		9 (3.1%)	
Other	401 (54.9%)	126 (68.1%)		94 (32.6%)	
Other LT health problems = yes	488 (65.1%)	103 (52.6%)	0.001[a]	125 (43.1%)	<0.001[a]
Other prescribed medication					
No	260 (35.2%)	81 (42.6%)	0.25[a]	125 (43.0%)	0.077[a]
Yes — one	177 (24.0%)	43 (22.6%)		76 (26.1%)	
Yes — two to three	191 (25.8%)	44 (23.2%)		56 (19.2%)	
Yes — four (+)	111 (15.0%)	22 (11.6%)		34 (11.7%)	
Seizures in past year					
None	191 (26.6%)	0	<0.001[a]	N/A	–
One to three	102 (14.2%)	21 (11.2%)			
Four+	426 (59.2%)	166 (88.8%)			
Median age first seizure (IQR)	19 (27)	16.5 (24)	0.024[c]	N/A	–
Median age most recent seizure (IQR)	44 (21)	43 (19)	0.066[c]	N/A	–
Aver. no. of seizures per month					
0	272 (36.2%)	18 (9.2%)	<0.001[a]	N/A	–
1–3	219 (29.2%)	68 (34.7%)			
4–5	79 (10.5%)	37 (18.9%)			
6+	145 (19.3%)	64 (32.7%)			
Seizure type					
Major	163 (21.7%)	33 (16.8%)	NS[a]	N/A	–
Both	316 (42.1%)	95 (48.5%)			
Other	228 (30.4%)	52 (26.5%)			
AEDs = yes	695 (92.5%)	192 (98.0%)	0.01[a]	N/A	–
No. of AEDs					
1	339 (50.7%)	62 (33.3%)	<0.001[a]	N/A	–
2	234 (35.0%)	85 (45.7%)			
3+	95 (14.2%)	39 (21.0%)			

[a] Chi-squared test.
[b] Kruskal–Wallis test.
[c] Mann–Whitney U-test.

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Table 4
Median scores for and prevalence of anxiety and sleep problems in PWE and controls.

	Epilepsy Action	Hospital	Controls	p-Value for differences between groups with epilepsy and controls
	n = 751	N = 196	n = 297	
State A total median (IQR)	46 (20)	47 (21)	35 (17.7)	<0.001[2]
Trait A total median (IQR)	50 (19)	49 (17.2)	39 (15)	<0.001[2]
PSQI total median (IQR)	9 (6)	7 (6)	7 (5)	<0.001[2,*]
Epworth total				
Normal	441 (59.1%)	120 (61.9%)	225 (76.3%)	<0.001[1]
Special advice	305 (40.9%)	74 (38.1%)	70 (23.7%)	
Health				
Excellent/very good	183 (24.5%)	42 (22.0%)	150 (51.4%)	<0.001[1]
Good	273 (36.5%)	60 (31.4%)	100 (34.2%)	
Fair/poor	291 (39.0%)	89 (46.6%)	42 (14.4%)	
Health cf. 1 year ago				
Better	185 (24.8%)	45 (23.6%)	57 (19.5%)	<0.001[1]
Same	349 (46.7%)	102 (53.4%)	198 (67.8%)	
Worse	213 (28.5%)	44 (23.0%)	37 (12.7%)	
AEP total				
Median (IQR)	47.5 (13)	46 (16)	35 (11)	<0.001[2]
Overall QOL				
Happy	375 (50.3%)	98 (50.3%)	225 (76.3%)	<0.001[1]
Neutral	128 (17.2%)	40 (20.5%)	29 (9.8%)	
Unhappy	242 (32.5%)	57 (29.2%)	41 (13.9%)	

[1] Chi-squared test.
[2] Kruskal–Wallis test.
[*] Difference between EA and hospital samples is also significant, $p < 0.001$.

Our second objective was to define the nature and extent of self-reported anxiety and sleep problems in our two separate cohorts of PWE. Comparing them, there was only one statistically significant difference in scores on the various measures described: the median PSQI score was higher for the EA sample than for the hospital sample ($p < 0.001$; see Table 4). State and trait anxiety scores were highly correlated with one another ($r = 0.74$) and were also moderately highly correlated with nighttime sleep problems (r for state anxiety and sleep = 0.40; r for trait anxiety and sleep = 0.39).

3.4. Factors contributing to anxiety and sleep problems in people with epilepsy

To achieve objectives 3 and 4, we considered factors contributing to scores for anxiety and sleep problems using both univariate and multivariate regression analyses. Since the two UK patient samples were shown to be clinically different, with the hospital sample representing individuals with more severe epilepsy, we considered each patient sample separately.

3.4.1. Univariate analysis

In a univariate analysis (data not shown, available on request from the authors), 11 factors were associated with *state* anxiety in both the EA- and hospital-based cohorts: gender, self-rated general health, worsening health compared to a year ago, having other long-term health problems, worry about past and possible future seizures, perceived level of seizure control, AEP score and level of compliance, perceived stigma, and level of social support. Ten common factors were associated with *trait* anxiety: self-rated general health, worsening health, other long-term health problems, worry about past and possible future seizures, perceived seizure control, AEP score and level of compliance, stigma, and level of social support. Nighttime sleep problems were associated with eight factors across both cohorts: self-rated general health and worsening health, having other long-term health problems, worry about past and possible future seizures, AEP score and level of compliance, and perceived stigma. Six factors were associated with daytime sleepiness in both cohorts: general health now and worsening health compared to a year ago, worry about past and possible future seizures, AEP score, and perceived stigma. Additionally, there were associations between the four dependent variables.

3.4.2. Multivariate analysis

Factors associated with the dependent variables were then entered into a multivariate (forward stepwise) regression analysis. For the EA sample, seven variables were predictive of state anxiety, accounting for 44% (adjusted $R^2 = 0.44$) of the variance in state anxiety scores (E-Table 1). Worse state anxiety was related to higher PSQI scores ($p < 0.001$), poorer general health ($p < 0.001$), higher AEP total scores ($p < 0.001$), greater worry about past seizures ($p < 0.001$), and worsening health ($p = 0.03$). In particular, patients with higher levels of state anxiety were four times as likely to describe their health as being fair or poor, five times as likely to report worrying significantly about past seizures, and more than twice as likely to consider their health worse now than a year ago. In contrast, increasing age ($p < 0.001$) and greater social support ($p < 0.001$) were shown to reduce the level of state anxiety. In the same sample, six variables accounted for 45% of the variance (adjusted $R^2 = 0.45$) in trait anxiety (E-Table 2). Worse trait anxiety was related to higher PSQI score ($p < 0.001$), higher AEP score ($p < 0.001$), and greater worry about past seizures ($p < 0.001$), whereas factors emerging as reducing the level of trait anxiety were general health as excellent or good ($p = 0.02$), older age ($p < 0.001$), and having greater social support ($p < 0.01$). In particular, patients with higher levels of trait anxiety were almost five times as likely to worry significantly about past seizures. Four variables – AEP score, stigma, level of treatment compliance, and state anxiety score – related to PSQI scores (E-Table 3), accounting for 29% of the score variance (adjusted $R^2 = 0.29$). Finally, just two factors, AEP score and age at first seizure, emerged as being significantly related to daytime sleepiness problems (E-Table 4), accounting for only 9% of the variance (Nagelkerke $R^2 = 0.09$).

In the multivariate regression analysis for the hospital-based sample, three variables were related to state anxiety, accounting for 40% (adjusted $R^2 = 0.40$) of the variance: AEP score, worry about possible future seizures, and perceived level of social support (E-Table 5). Patients with higher levels of state anxiety were more than 10 times as likely to worry significantly about possible future seizures ($p < 0.001$). In the same sample, six variables accounted for 46% of the variance (adjusted $R^2 = 0.46$) in trait anxiety: AEP score, worry about possible future seizures, AED treatment compliance, levels of social support, perceived stigma, and age at the time of the most recent seizure (E-Table 6). Patients with higher levels of trait anxiety were almost five times as likely to worry significantly about possible future seizures

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($p = 0.005$) and almost three times as likely to be treatment-compliant ($p < 0.001$). Three variables – AEP total score, other long-term health problems, and state anxiety score – related to PSQI scores (E-Table 7), accounting for 27% of the score variance (adjusted $R^2 = 0.27$). Only one factor, AEP total score, emerged as significant for daytime sleepiness problems (E-Table 8), accounting for 19% of the variance (Nagelkerke $R^2 = 0.19$).

3.5. Relationship of reported anxiety and sleep problems to QOL of people with epilepsy

To address objective 5, we examined the relationship between our four dependent variables, other possible predictive variables, and overall QOL of our two samples with epilepsy. Six factors emerged as significant for overall QOL in the EA sample (Table 5): reported trait anxiety and nighttime sleep problems, lower levels of social support, feeling severely stigmatized, worry about possible future seizures, and seizures in the past year. Together, these six factors accounted for 52% of the variance for overall QOL (Nagelkerke $R^2 = 0.52$). Only three factors were significantly related to overall QOL in the hospital sample (Table 6): reported trait anxiety, lower social support, and poorer general health, accounting for 49% of the variance for overall QOL (Nagelkerke $R^2 = 0.49$).

4. Discussion and conclusions

Given the current emphasis on the role of psychological comorbidities for determining quality-of-life outcomes in epilepsy [56–58], there is a need to better understand the role of anxiety and sleep problems. The study reported here is one of few to look at the prevalence of self-reported anxiety and sleep problems in a large cohort of people with epilepsy matched to controls. It is the only study, to our knowledge, that has used, as the measure of anxiety, the State–Trait Anxiety Inventory which separately assesses these two related but independent dimensions and so provides unique data on the nature of anxiety of people with epilepsy. The data presented add to our understanding of the compound nature of anxiety in PWE and the factors predictive of its two separate dimensions. Our study confirms an increased prevalence of self-reported anxiety, both state and trait, in people with epilepsy compared to matched controls. The differences are consistent with normative data for the STAI, which show, both for state anxiety and trait anxiety, an approximate 10-point difference between scores for healthy working adults and patients with neuropsychiatric problems [46]. Spielberger's argument that state anxiety is a function of more immediate life stressors is supported by the finding that state, but not trait, anxiety was associated with self-reported worsening health over the previous year (for the EA sample) and worrying about possible seizure recurrence (for the hospital sample). However, there were also common contributory factors for the two separate dimensions of anxiety — experiencing AED side effects contributed to increased state and trait anxiety and, conversely, good social support emerged as a protective factor for both dimensions in both samples with epilepsy.

Nighttime sleep problems are very common even in normal populations [59] but are shown in our study to be further elevated in populations of people with epilepsy. Four-fifths of those with epilepsy in this study reported nighttime sleep difficulties and two-fifths reported daytime sleepiness. This compares to only a fifth of the control population. Antiepileptic drugs have been viewed as beneficial in treating some anxiety disorders in PWE [24,60], and it has been documented that AED withdrawal can increase anxiety problems [61]. However, in the present study, experiencing problems with AED adverse events emerged as an important contributory factor not only for anxiety but also for sleep problems in both our samples of people with epilepsy, reemphasizing the importance of addressing patient-reported adverse effects robustly.

Few studies previously have addressed the impact of anxiety on QOL [62], and those that have done so have generally involved small numbers of patients [19,56,63]. Our own study involved large numbers of both PWE and controls and considered the role not just of anxiety but also of its less investigated concomitant, sleep problems, for QOL overall. Not only did those with epilepsy experience increased rates of anxiety and sleep problems, but they were also more likely to report poor general health and worse health now than a year ago than were the controls. Though study participants were not asked to define the precise physical conditions that they suffered from, this finding parallels those of Tellez-Zenteno et al. [64] who reported people with epilepsy participating in the Canadian National Health Survey as having higher rates of comorbid physical disorders, including possibly stress-related ones, and Strine et al. [14] who reported higher rates of psychological distress including nervousness, hypersomnia, and insomnia among PWE than the general US population. Given our own findings, it is unsurprising that the people with epilepsy in this UK-based study reported poorer quality of life overall. Only one-half of the patient samples with epilepsy described themselves as happy with their quality of life compared to three-quarters of controls.

In our analysis, trait, though not state, anxiety emerged as a significant contributor to overall quality of life of people with epilepsy. This is consistent with Spielberger's [46] finding that high trait anxiety scores are associated with a larger number of self-reported problems in almost every area of life adjustment, with those who are anxiety-prone reporting problems in many areas of daily function including health, social and intimate relationships, educational and work adjustment, and future planning — a finding with important practical implications in relation to clinical management of people with epilepsy. The

Table 5
Factors predicting overall QOL for the EA sample.

Variable	Exp(coefficient)	Significance	95% confidence interval
Trait	0.89	<0.001	(0.87, 0.91)
PSQI	0.94	0.02	(0.89, 0.99)
Support			
Low	0.31	0.01	(0.16, 0.61)
Medium	1.00	0.03	(1.04, 2.60)
High	1.65		
Stigma			
None	1.34	NS	(0.82, 2.19)
Moderate	1.00	0.01	(0.06, 0.50)
Severe	0.17		
Worried might have another seizure			
Very/fairly	0.64	0.04	(0.42, 0.98)
Little/not	1.00		
Seizures (in past year)			
None	1.00	0.03	(1.09, 4.60)
1–3	2.24	NS	(0.81, 2.19)
4+	1.33		
Constant	6.17	<0.001	

Table 6
Factors predicting overall QOL for the hospital sample.

Variable	Exp(coefficient)	Significance	95% confidence interval
Trait	0.90	<0.001	(0.87, 0.94)
Support			
Low	0.17	0.06	(0.03, 1.08)
Medium	1.00	NS	(0.33, 1.90)
High	0.80		
General health			
Excellent/very good	1.12	NS	(0.73, 1.72)
Good	1.00	<0.001	(0.22, 0.47)
Fair/poor	0.33		
Constant	405.03	<0.001	

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importance of trait over state anxiety in our study supports the notion of anxiety in PWE as a primarily premorbid rather than reactive condition, perhaps with common risk factors and linked to previously learned coping styles as has been increasingly recognized for comorbid depression [65]. The need to categorize the full range of comorbidities, explore their underlying mechanisms, and build an evidence base for their treatment has been highlighted [66].

In contrast, sleep quality was not consistently independently associated with or predictive of overall quality of life among our patient groups. Our findings, therefore, parallel those of Kwan et al. [67] who explored QOL in a Chinese cohort of people with epilepsy and found that though both anxiety and sleep disorder were independently predictive of reduced QOL, anxiety emerged as having the greatest impact. The study also goes some way towards identifying the nature, frequency, and extent of self-reported sleep problems, which it suggests are partly the outcome of taking antiepileptic medications, and their relationship to anxiety. This again has clinical management implications of which clinicians may not always be cognizant. Clinicians treating PWE need to be vigilant for both of these important comorbidities, which clearly influence the day-to-day lives of those concerned.

Finally, we would emphasize the important positive role of social support for the reduction of anxiety and sleep problems as evidenced in our study. This supports previous work providing clear evidence of the protective effects of this and other external factors, including for psychological well-being, among both people with [68] and people without [69,70] epilepsy.

4.1. Study limitations

In the analyses presented here, we have provided data for the two cohorts with epilepsy separately, our reasoning being that since the hospital sample presented as having clinically more severe epilepsy, they might therefore be expected to have a worse psychosocial profile and more impaired QOL than those recruited from the patient support group. We recognize that there may be some overlap across the samples since patient organizations such as EA typically attract members from patients with more severe epilepsy who are likely being treated in hospital-based clinics. Notwithstanding this potential confounder, our analysis highlights that while rates of anxiety and sleep problems are similar and there are commonalities in predictive factors for these comorbidities in question across the two groups, there are also clear differences (as shown in E-Tables 1–8). We would suggest that these findings emphasize the need for clinicians to be aware of such potential differences across different patient groups since they will likely have implications for their clinical management.

There are a number of other limitations with the work that we report. The first of these is that those PWE identified via the UK patient support group were self-selecting, and as such, the sample was open to bias — as highlighted above, evidence suggests that such support groups may attract patients for whom psychosocial management and QOL issues are particularly acute. Our hospital-based sample was identified using prespecified sampling criteria and, unlike the EA sample, was sent reminders to participate. Nonetheless, the response rate from this group was relatively low, at only 36%, presenting another source of bias. Further, we had no control over whether or not our samples with epilepsy approached age- and gender-matched controls, as requested, nor were we able to send out reminders to controls. In relation to this, although we employed a postal approach for data collection, we supplemented this for EA members by providing the option to complete the survey online, and a small number of participants did so. Previous research suggests that the quality of data obtained using different survey approaches is broadly similar, with research participants appearing to respond to the content of the questions rather than the mode of administration [42,71], but we acknowledge that the lack of a consistent approach is potentially problematic.

In examining the prevalence of anxiety and sleep problems in our study populations, we were dependent on self-report rather than clinical assessment. Kanner and Ettinger [72] note that such self-rated instruments do not establish diagnoses even though they represent a useful initial approach, and they caution that though several instruments are available, they have not been validated for use in epilepsy. Nonetheless, evidence suggests that self-reports do reflect clinical experience of anxiety [49,73]. Despite the caveats that they make, Kanner and Ettinger themselves suggest a number of possible self-rated instruments, including HADS [74], which we have used in a number of previous studies of QOL. We are unaware of other studies where the STAI has been used, though general population norms for the STAI provide useful comparative data. However, both the STAI and the sleep scales that we used are well validated and have been widely used in both clinical research and epidemiological studies (Table 1).

The interpretation of our findings is limited by the fact that we did not collect information about comorbid depression in our samples. That there is a large overlap between anxiety and depression is well documented in people with and without epilepsy [62,75], and we recognize that inclusion of a measure of depression could have been highly instructive. Future work could usefully explore this set of interrelationships in greater detail.

4.2. Final conclusions

In conclusion then, further research is needed but it is abundantly clear that levels of psychological morbidity, including anxiety and sleep problems, need to be considered when establishing epilepsy treatment regimes [19] and that subjective symptoms of anxiety and sleep problems as well as depression and other epilepsy variables require simultaneous consideration when evaluating effects of treatment on QOL [67]. In particular, trait anxiety emerged as of particular importance in relation to overall QOL. That clinical epilepsy factors contributed little to QOL overall in the present study population is consistent with our own [4] and others' [76] previous reports and has important clinical management implications, emphasizing the need for a holistic approach to address wider patient-reported problems as well as any epilepsy-specific ones.

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Conflict of interest

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Aventis, and UCB Pharma. Neither of the other authors have any conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article and copies of the STAI, PSQI and ESS items can be found online at http://dx.doi.org/10.1016/j.yebeh.2014.09.071.

References

[1] Jacoby A, Ring A, Whitehead M, Marson A, Baker GA. Exploring loss and replacement of loss for understanding the impacts of epilepsy onset: a qualitative investigation. Epilepsy Behav 2014;33:59–68.
[2] Baker GA, Jacoby A, Chadwick DW. The associations of psychopathology in epilepsy: a community study. Epilepsy Res 1996;25:29–39.
[3] Jacoby A. Epilepsy and the quality of everyday life, findings from a study of people with well controlled epilepsy. Soc Sci Med 1992;34(6):657–66.
[4] Jacoby A, Baker GA, Steen N, Potts P, Chadwick DW. The clinical course of epilepsy and its psychosocial correlates: findings from a UK community study. Epilepsia 1996;37(2):148–61.
[5] Leidy NK, Elixhauser A, Vickrey E, Means E, Willian MK. Seizure frequency and the health related quality of life of adults with epilepsy. Neurology 1999;53:162–6.
[6] Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Quality of life of people with epilepsy: a European study. Epilepsia 1997;38(3):353–62.
[7] Jacoby A, Lane S, Marson A, Baker GA. Relationship of clinical and quality of life trajectories following the onset of seizures: findings from the UK MESS Study. Epilepsia 2011;52(5):965–74.
[8] Spenser SS, Berg AT, Vickrey B, Sperling MR, Bazil CW, Haut S, et al. Health-related quality of life over time since resective epilepsy surgery. Ann Neurol 2007;62(4):327–34.
[9] Poochikian-Sarkissian S, Sidani S, Wennberg R, Devins GM. Seizure freedom reduces illness intrusiveness and improves quality of life. Can J Neurol Sci 2008;35:280–6.
[10] Smith DF, Baker GA, Dewey M, Jacoby A, Chadwick DW. Seizure frequency, patient perceived seizure severity and the psychosocial consequences of intractable epilepsy. Epilepsy Res 1991;9:231–41.
[11] Torta R, Keller R. Behavioural, psychotic, and anxiety disorders in epilepsy: etiology, clinical features and therapeutic implications. Epilepsia 1999;40(Suppl. 10):S2–S20.
[12] Piazzini A, Canevini MP, Maggiori G, Canger R. Depression and anxiety in patients with epilepsy. Epilepsy Behav 2001;2:481–9.
[13] Perucca P, Carter J, Vehle V, Gilliam FG. Adverse antiepileptic drug effects: towards a clinically and neurobiologically relevant taxonomy. Neurology 2009;72(4):1223–9.
[14] Strine TW, Kobau R, Chapman DP, Thurman DJ, Price P, Balluz LS. Psychological distress, comorbidities and health behaviours among US adults with seizures: results from the 2002 National Health Interview Survey. Epilepsia 2005;46:1133–9.
[15] Pulsipher DT, Seidenberg M, Jones J, Hermann B. Quality of life and co-morbid medical and psychiatric conditions in temporal lobe epilepsy. Epilepsy Behav 2006;9:510–4.
[16] Fiordelli E, Beghi E, Bogliun G, Crespi V. Epilepsy and psychiatric disturbance, a cross-sectional study. Br J Psychiatry 1983;163:446–50.
[17] Gaitatzis A, Carroll K, Majeed A, Sander JW. The epidemiology of the comorbidity of epilepsy in the general population. Epilepsia 2004;45(12):1613–22.
[18] Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its association with self-reported depression and anxiety: results from the 2004 HealthStyles Survey. Epilepsia 2006;47(11):1915–21.
[19] Johnson EK, Jones JE, Seidenberg M, Hermann BP. The relative impact of anxiety, depression and clinical seizure features on health related quality of life in epilepsy. Epilepsia 2004;45(5):544–50.
[20] Cramer JA, Brandenburg N, Xu X. Differentiating anxiety and depression symptoms in patients with partial epilepsy. Epilepsy Behav 2005;6:563–9.
[21] Tellez-Zenteno JF, Patten SB, Jette N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia 2007;48(12):2336–44.
[22] Mensah SA, Beavis JM, Thapar AJ, Kerr MP. A community study of the presence of anxiety disorder in people with epilepsy. Epilepsy Behav 2007;11:118–24.
[23] O'Donoghue MF, Goodridge DM, Redhead K, Sander JW, Duncan JS. Assessing the psychosocial consequences of epilepsy: a community-based study. Br J Gen Pract 1999;49:211–4.
[24] Beyenberg S, Mitchell AJ, Schmidt D, Elger CE, Reuber M. Anxiety in patients with epilepsy: systematic review and suggestions for clinical management. Epilepsy Behav 2005;7:161–71.
[25] Schmitz B. Psychiatric issues. In: Schmidt D, Schachter S, editors. Epilepsy: problem solving in clinical practice. London: Martin Dunitz; 2000. p. 169–90 [Chpt 13].
[26] Marsh L, Rao V. Psychiatric complications in patients with epilepsy: a review. Epilepsy Res 2002;49:11–33.
[27] De Souza EAP, Salgado PCB. A psychosocial view of anxiety and depression in epilepsy. Epilepsy Behav 2006;8:232–8.
[28] Schmitz B. Effects of antiepileptic drugs on mood and behavior. Epilepsia 2006;47(Suppl. 2):S28–33.
[29] Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
[30] Sander JW. Ultimate success in epilepsy — the patient's perspective. Eur J Neurol 2005;12(Suppl. 4):3–11.
[31] Mendez M, Radtke RA. Interactions between sleep and epilepsy. J Clin Neurophysiol 2001;18(2):106–27.
[32] Bazil CW. Epilepsy and sleep disturbance. Epilepsy Behav 2003;4(Suppl. 2):S39–45.
[33] De Haas S, de Weerd, Otte A, et al. Epidemiology of sleep disturbance in patients with partial seizures. Paper presented at: 5th European Congress on Epileptology (ECE). October 6-10, 2002, Madrid, Spain.
[34] Jenkins CD, Stanton BA, Niemcryk SJ, Rose M. A scale for estimation of effects of treatment on sleep problems. J Clin Epidemiol 1988;41:313–21.
[35] Hermann BP, Seidenberg M, Bell B. Psychiatric comorbidity in chronic epilepsy: identification, consequences and treatment of major depression. Epilepsia 2000;41(Suppl. 2):S31–41.
[36] Hermann BP. Quality of life in epilepsy. J Epilepsy 1992;5:153–65.
[37] Fisher RS, Vickrey BG, Gibson P. The impact of epilepsy from the patient's perspective I: descriptions and subjective perceptions. Epilepsy Res 2000;41:39–51.
[38] Xu X, Brandenburg NA, McDermott AM, Bazil CW. Sleep disturbances reported by refractory partial-onset epilepsy patients receiving polytherapy. Epilepsia 2006;47:1176–83.
[39] De Weerd A, de Haas S, Otte A, Trenite DKJ, Erp G, Cohen A, et al. Subjective sleep disturbance in patients with partial epilepsy: a questionnaire-based study on prevalence and impact on quality of life. Epilepsia 2004;45(11):1397–2004.
[40] Malow BA, Bowes RJ, Lin X. Predictors of sleepiness in epilepsy patients. Sleep 1997;20:1105–10.
[41] Piperidou C, Karlovasitou A, Triantafyllou N, Terzoudi A, Constantinidis T, Vadikolias K, et al. Influence of sleep disturbance on quality of life of patients with epilepsy. Seizure 2008;17:588–94.
[42] McColl E, Jacoby A, Thomas L, Soutter J, Bamford C. Design and use of questionnaires: a review of best practice applicable to surveys of health service staff and patients. HTA 2001;5(31).
[43] Jacoby A, Baker GA, Smith D, Dewey M, Chadwick DW. Measuring the impact of epilepsy: the development of a novel scale. Epilepsy Res 1993;16(1):83–8.
[44] Jacoby A, Gamble C, Doughty J, Marson A. Quality of life outcomes of immediate or delayed treatment of early epilepsy and single seizures. Neurology 2007;68:1188–96.
[45] Baker GA, Jacoby A, Gorry J, Doughty J, Ellina V. Quality of life of people with epilepsy in Iran, the Gulf and Near East. Epilepsia 2005;46(1):132–40.
[46] Spielberger CD, Gorsuch RL, Luschene RE, Vagg PR, Jacobs GA. Manual for the State–Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
[47] Spielberger C. Anxiety: current trends in research. London: Academic Press; 1972.
[48] Spielberger CD. Manual for the State–Trait Anxiety Inventory STAI (Form Y). Palo Alto, CA: Consulting Psychologists Press; 1983.
[49] Guillér-Riquelme A, Buela-Casal G. Meta-analysis of group comparisons and meta-analysis of reliability generalisations of the State Trait Anxiety Inventory questionnaire (STAI). Rev Esp Salud Publico 2014;88(1):101–12.
[50] Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14:540–5.
[51] Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992;15(4):376–81.
[52] Gilliam F, Fessler AJ, Baker G, Vahle V, Carter J, Attarian H. Systematic screening allows reduction of adverse antiepileptic drug effects: a randomized study. Neurology 2004;62:6–7.
[53] Jacoby A. Felt versus enacted stigma: a concept revisited. Evidence from a study of people with epilepsy in remission. Soc Sci Med 1994;38(2):269–74.
[54] Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32(6):705–14.
[55] Abetz L, Jacoby A, Baker GA, McNulty P. Patient-based assessment of quality of life in newly diagnosed epilepsy patients: validation of the NEWQOL. Epilepsia 2000;41(9):1119–28.
[56] Kanner AM, Wuu J, Barry J, Hermann B, Meador KJ, Gilliam F. Atypical depressive episodes in epilepsy: a study of their clinical characteristics and impact on quality of life. Neurology 2004;62(Suppl. 5):A249.
[57] Loring DW, Meador KJ, Lee GP. Determinants of quality of life in epilepsy. Epilepsy Behav 2004;5:976–80.
[58] Schachter SC. Quality of life for patients with epilepsy is determined by more than seizure control: the role of psychosocial factors. Exp Rev Neurother 2006;1:111–8.
[59] Sie M. An update on sleep disorders and their treatment. Prog Neurol Psychiatry 2013;17(5):15–23.
[60] Boylan LS, Devinsky O, Barry JJ, Ketter TA. Psychiatric uses of antiepileptic treatments. Epilepsy Behav 2002;3a(5S):54–9.
[61] Ketter TA, Post RM, Theodore WH. Positive and negative psychiatric effects of antiepileptic drugs in patients with seizure disorders. Neurology 1999;53(Suppl. 5):S53–67.
[62] Thapar A, Kerr M, Harold G. Stress, anxiety, depression and epilepsy: investigating the relationship between psychological factors and seizures. Epilepsy Behav 2009;14:134–40.
[63] Choi-Kwon S, Chung C, Kim H, Lee S, Yoon S, Kho H, et al. Factors affecting the quality of life in patients with epilepsy in Seoul, South Korea. Acta Neurol Scand 2003;108–42.
[64] Tellez-Zenteno JF, Matijevic S, Wiebe S. Somatic comorbidity of epilepsy in the general population in Canada. Epilepsia 2005;46:1955–62.
[65] Hesdorffer DC, Lee P. Health, wealth and culture as predominant factors in psychosocial morbidity. Epilepsy Behav 2009;15:S36–40.
[66] Austin J. The 2007 Judith Hoyer lecture. Epilepsy comorbidities: Lennox and lessons learned. Epilepsy Behav 2009;14:3–7.

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[67] Kwan P, Yu E, Leung H, Leon T, Mychaskiw MA. Association of subjective anxiety, depression, and sleep disturbance with quality of life rating in adults with epilepsy. Epilepsia 2008;50:1059–66.
[68] Amir M, Roziner I, Knoll A, Neufield MY. Self-efficacy and social support as mediators in the relation between disease severity and quality of life in patients with epilepsy. Epilepsia 1999;40:216–24.
[69] Stansfeld SA, Rael EGA, Head J, Shipley M, Marmot M. Social support and psychiatric sickness absence: a prospective study of British civil servants. Psychol Med 1997;27:35–48.
[70] Seeman TE, Berkman CF, Blazer D, Rowe JW. Social ties and support as modifiers of neuroendocrine function: the MacArthur studies of successful aging. Ann Behav Med 1994;16:95–106.
[71] Gil KM, Frasure HE, Hopkins MP, Jenison EL, von Gwenigen VE. Effect of method of administration on longitudinal assessment of quality of life in gynaecological cancer: an exploratory study. Health Qual Life Outcomes 2005;3:6. http://dx.doi.org/10.1186/1477-7525-3-6.
[72] Kanner AM, Ettinger AB. Chapter 206: anxiety disorders. In: Engel Jr J, Pedley TA, editors. Epilepsy: a comprehensive textbook, 2nd Edition, vol. 3. Philadelphia: Lippincott Williams & Wilkins; 2008.
[73] Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale, an updated literature review. J Psychosom Res 2002;52:69–77.
[74] Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psych Scand 1983;67:361–70.
[75] Hettema JM, Kuhn JW, Prescott CA, Kendler KS. The impact of generalised anxiety disorder and stressful life events on risk for major depressive episodes. Psychol Med 2006;36:789–95.
[76] Hermann BP, Whitman S. Psychopathology in epilepsy: a multi-etiological model. In: Whitman S, Hermann BP, editors. Psychopathology in epilepsy: social dimensions. Oxford: OUP; 1986. p. 5–37.

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